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TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTEO OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371 INTERNATIONAL APPLICATION NO. INTERNATIONAL FILING DATE PCT/GB0/03332 31 August 2000 03 September 1999 HIGH DYNAMIC RANGE MASS SPECTROMETER APPLICANT(S) FOR DO/EO/US Slephen DAVIS, Alexander MAKAROV; and Jonathan HUGHES Rephen DAVIS, Alexander MAKAROV; and Jonathan HUGHES Rephen DAVIS, Alexander MAKAROV; and Jonathan HUGHES Slephen DAVIS, Alexander MAKAROV; and Jonathan HUGHES Applicant brewith submits to the United States Designate/Elected Office (DO/EO/US) the following items and other information: 1. **Extra **E	FORM PTO- (REV 11-20	1390 US DEPARTMENT OF COM	MERCE PATENT AND TRADEMARK OFFICE	ATTORNEY 'S DOCKET NUMBER
DESIGNATED/ELECTED OFFICE (DO/EC/US) CONCERNING A FILING UNDER 35 U.S.C. 371 INTERNATIONAL APPLICATION NO. INTERNATIONAL FILING DATE PCT/GB00/03332 TITLE OF INVENTION HIGH DYNAMIC RANGE MASS SPECTROMETER APPLICANTIS, FOR DO/EO/US Slephen DAVIS, Alexander MAKAROV, and Jonathan HUGHES Applicant hrewth submiss to the United States Designated/Biceted Office (DO/EO/US) the following items and other information: 1. This is a FIRST submission of items concerning a filing under 35 U.S.C. 371. 2. This is an express request to begin antional examination procedures (33 U.S.C. 371(f)). The submission must include items (5), (6), (9) and (21) indicated below? Hornor of the International Application as filed (35 U.S.C. 371(e), (21) a. is attached hereto (required only if not communicated by the International Bureau). b. has been communicated by the International Bureau. c. ji is not required, as the application was filed in the United States Receiving Office (RO/US). 6. A compton of the International Application as filed (35 U.S.C. 371(e)(2)). a. W is attached hereto. b. has been previously submitted under 35 U.S.C. 154(d)(4). 7. Mamendments to the claims of the International Bureau. c. have not been made; however, the time limit for making such amendments has NOT expired. d. W have not been made and will not be made. 8. An English language translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371 (c)(3)). 9. An oath or declaration of the international Bureau. c. have not been made; however, the time limit for making such amendments has NOT expired. d. W have not been made and will not be made. 8. An English language translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371 (c)(3)). 9. An oath or declaration of the international Bureau. c. have not been made and will not be made. 8. An English language translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371 (c)(3)). 10. A Particle 30 (35 U.S.C. 371 (c)(5)). 11. An Information Disclosur	í		TO THE UNITED STATES	J318-094 US
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Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information: 1.			and longthan HUGHES	
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21. The following fees are submitted:					CAI	CULATIONS 1	PTO USE ONLY
BASIC NATIONAL	-		(1) - (5)):				
Neither internation	al preliminary ex	aminati	on fee (37 CFR 1.482)				
nor international se and International S	arch fee (37 CFR earch Report not)	1.445(prepare	a)(2)) paid to USPTO d by the EPO or JPO	\$1000.00			
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Independent claims	2 -3	==	0	x \$80.00	\$ o		
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			SU	JBTOTAL =	\$ 8	90.00	<u> </u>
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						charged:	\$
a. X A check in the amount of \$ 890.00 to cover the above fees is enclosed.							
b. Please charge my Deposit Account No in the amount of \$ to cover the above fees. A duplicate copy of this sheet is enclosed.							
c. [x] The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any							
overpayment to Deposit Account No. 14-1431 . A duplicate copy of this sheet is enclosed.							
d. Fees are to be charged to a credit card. WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.							
NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137 (a) or (b)) must be filed and granted to restore the application to pending status.							
SEND ALL CORRESPONDENCE TO							
Notaro & Michalos P.C.					RE	-	
100 Dutch Hill Road, Suite 110						Michalos	
Orangeburg, New York 10962-2100 Phone No.: 845-359-7700 NAME					<u>U.</u>	MICHAIUS	
Dated: January 30, 2002 28,64					L3		
CUSTOMER NO.: 21706						MINADER	
	VIA EXPRESS MAIL LABEL NO.: EV 063136319 US						

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Patent

Atty. Docket: J318-094 US

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant

: Stephen Davis, et al

Serial No.

N/A

Filing Date

Concurrently Herewith

Examiner

N/A

Group Art Unit

N/A

For

HIGH DYNAMIC RANGE MASS SPECTROMETER

Intl. Appln. No.

PCT/GB00/03332

Intl. Filing Date

August 31, 2000

Box PCT

Commissioner for Patents Washington, D.C. 20231

PRELIMINARY AMENDMENT

Sir:

Prior to examination, please amend the above-identified application, as follows:

IN THE CLAIMS:

Please cancel Claims 3, 4, 5, 6, 8 and 11.

Please add the following new Claims 15-20.

- --15. A mass spectrometer according to Claim 1, wherein each detector element comprises a separate plate anode.
- 16. A mass spectrometer according to Claim 1, wherein each detector element is connected via an amplified to a time to digital converter (TDC) to allow counting of detected ions.
- 17. A mass spectrometer according to Claim 1, wherein the detector elements are disposed one behind the other relative to the ion source.
- 18. A mass spectrometer according to Claim 1, wherein the detector elements are disposed one above the other in a plane extending generally perpendicular to the direction of ion travel.
- 19. A mass spectrometer according to Claim 1, wherein the attenuation means is formed by at least one of the detector elements.
- 20. A mass spectrometer according to Claim 1, wherein said attenuation device is provided between the ion source and the detector elements which acts to reduce the number of ions reaching at least one of said elements or at least a part thereof. –

REMARKS

Claims 1, 2, 7, 9, 10 and 12-20 are in the application, and presented for consideration.

By this amendment, applicants have deleted reference to improper multiple dependent claims only.

No new matter has been added.

Entry of the Preliminary Amendment is, therefore, respectfully requested.

Respectfully submitted,

Peter C. Michalos Reg. No. 28,643

Attorney for Applicant(s)

(845) 359-7700

Dated:

NOTARO & MICHALOS P.C.

100 Dutch Hill Road

Suite 110

Orangeburg, New York 10962-2100

CUSTOMER NO.: 21706

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10/070118 PCT/GB00/03332 PTO/PCT Rec'd 01 MAR 2002

-1-

HIGH DYNAMIC RANGE MASS SPECTROMETER

This invention relates to a high dynamic range mass spectrometer, preferably although not exclusively of the time of flight kind.

Time of flight (TOF) mass spectrometers are often used for quantitative analysis of substances. In these applications of a TOF mass spectrometer, it will be necessary to be able to accurately determine the concentration of a substance based upon a detected ion signal. In a TOF mass spectrometer, the ion signals which are to be detected are usually fast transients and can be measured by analogue to digital conversion using a transient recorder or by ion counting as a function of time using a time to digital convertor (TDC). Use of a TDC is generally preferred because it can be more difficult to obtain accurate quantitative results using a transient recorder. The use of ion counting is further preferred in an orthogonal acceleration TOF because the signals to be measured tend to be small and the ion count rates are low. Ion counting using a TDC involves the TDC detecting the presence of a signal at the detector in excess of a predetermined threshold. If the signal detected is in excess of a predetermined threshold then this is deemed to be indicative of the presence of an ion at the detector and the TDC, after detection of the above threshold signal, increments a counter to count the ions.

However, a problem arises with a time to digital convertor when this is used to count ions in intense ion beams because most TDC's can only

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detect one event in a finite small time window. This means that where a TDC is used, it is not normally possible to distinguish between a single ion being detected and a multiplicity of ions being detected at the same time. This arises because a TDC cannot distinguish between different magnitudes of signal, only whether the detected signal exceeds the predetermined threshold. Accordingly, a counter connected to the TDC will only be incremented once upon detection of an above threshold signal regardless of its magnitude and therefore in the case of intense ion beams an accurate quantitative measurement cannot be made. This means that mass spectrometers incorporating such ion counters usually require there to be less than or equal to one ion per signal pulse of any substance to measured. It also means that for a single TDC there will be a relatively low dynamic range.

Attempts have been made to provide a mass spectrometer which uses one or more TDC's to count ions and in which the dynamic range can be extended for better quantitative measurements.

Thus for example, U.S. Patent No. 5,777,326 discloses a TOF mass spectrometer in which the incoming ion beam is spread so as to be capable of being detected by three or more detectors. The signal at each detector is detected by a respective TDC and the signal from each TDC is subsequently added together. However, the problem with this type of arrangement is that simply spreading the beam over a number of detectors

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does not affect the intensity of the beam to a sufficient extent to significantly enhance dynamic range without a very large number of TDC's.

It is an object of the present invention to provide an alternative form of mass spectrometer in which ion counting can be used to cover a wide dynamic range using a small number of TDC's.

Thus and in accordance with the present invention therefore there is provided a mass spectrometer comprising a mass spectrometer comprising an ion source to produce ions from a substance to be detected and detector means to detect a quantity of ions incident on said detection means wherein the said detection means includes at least two detector elements, each of which elements detect at least a part of said quantity of ions from the ion source and attenuation means which acts to attenuate the quantity of ions reaching at least one said detection element, wherein at least one of said detection elements is connected to a time-to-digital converter (TDC) to allow counting of detected ions and at least one of said detection elements is connected in parallel to both a time-to-digital converter (TDC) and an analogue-to-digital converter (ADC) for ion detection.

With this arrangement it is possible to measure the quantity of ions with and without attenuation which means that both single and multiple ion detections can be quantified more accurately and a high dynamic range for the mass spectrometer can be achieved. This is achieved by parallel acquisition or interleaved acquisition of signal from ion beams with

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significant attenuation at one detector element and almost no attenuation at another.

Although the discussion has been in terms of using TDC acquisition it will be appreciated that the same principle of attenuation of signal to other detector elements could also be applied to extension of dynamic range using analogue-to-digital conversion (ADC) or combinations of TDC and ADC.

The detector elements may be disposed one behind the other relative to the ion source or alternatively may be disposed one above the other in a plane extending generally perpendicular to the direction of ion travel. In the case where the detector element is disposed one behind the other, an earthed member preferably a wire or grid may be provided between the elements to minimise capacitative coupling between these elements.

The attenuation means may be performed by at least one of the detector elements and in this case the at least one detector element is adapted to allow a proportion of incident signal to pass through the element without being detected. The adaptation may comprise a plurality of perforations or other apertures in the element. Alternatively a separate attenuation device may be provided between the ion source and the detector elements which acts to reduce the number of ions reaching at least one of said elements or at least a part thereof. In these circumstances the attenuation device may comprise a perforated plate.

Preferably, in the case where the attenuation means is formed by a

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perforation of the detector element, the cross-sectional area of the perforations compared to the total cross-sectional area of the plate is substantially 1 to 100.

The invention will now be described further by way of example and with reference to the accompany drawings of which:-

Fig. 1 shows a schematic version of a prior art form of mass spectrometer;

Fig. 2 shows a schematic version of one embodiment of mass spectrometer;

Fig. 3 shows a variation on the embodiment shown in Fig. 2;

Fig. 4 shows a schematic version of a second embodiment of mass spectrometer;

Fig. 5 shows a schematic version of a third embodiment of mass spectrometer;

Fig. 6 shows a schematic version of a fourth embodiment of mass spectrometer in accordance with the present invention; and

Fig. 7 shows a schematic version of a fifth embodiment of mass spectrometer in accordance with the present invention.

Referring now to the drawings, there is shown in Fig. 1 a schematic representation of one standard form of prior art mass spectrometer detector. The spectrometer 10 comprises an ion source (not shown) which produces an ion beam from a substance to be analysed. The ion beam is directed by conventional means onto a pair of microchannel plates 11,12 (hereinafter

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referred to as a chevron pair) which generates secondary electrons due to the collision of the ions in the ion beam with the material of the plates 11,12 in the microchannels. Secondary electrons generated are detected by a single plate anode 13, the detected signal is amplified in an amplifier 14 and is passed to a time to digital convertor (TDC) (not shown) which detects detected signals over a predetermined threshold and increments a counter to count these above threshold signals.

This form of mass spectrometer suffers from the problem that if an above threshold signal is detected by the TDC, the counter will be incremented only once regardless of the magnitude of the signal in exceeding the threshold. Thus even if the signal is of such a magnitude as to constitute more than one ion being detected, the counter will still only be incremented once. The TDC cannot distinguish between different magnitude above threshold signals. This means that the mass spectrometer is very inaccurate when used for quantitative measurements of intense signals.

One form of mass spectrometer in accordance with the present invention is shown in schematic form in Fig. 2. In this arrangement, the ion beam generated by the ion source (not shown) is also incident on a chevron pair 11,12 as with the embodiment of Fig. 1. The ion beam strikes the microchannel plate 11 and causes the ejection of secondary electrons from the surface of the microchannels. The secondary electrons cause the

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ejection of further secondary electrons as they accelerate through the microchannels in the plates 11,12 which results in an electron beam which emerges from the chevron pair 11,12 being essentially an amplified signal version of the incoming ion beam. The secondary electron beam then strikes a first anode 16 for detection. The first anode 16 is perforated in order that some of the secondary electrons pass through the first anode 16 without being detected. The remainder of the secondary electrons strike the first anode 16 and are detected. For detection purposes, the first anode 16 is connected to an amplifier 14 and to a time to digital converter (not shown) the output of which increments a counter (not shown) as previously explained. Those secondary electrons which pass through the perforations 17 in the first anode 16 strike a second anode 18 placed substantially immediately behind the first anode 16 and are detected. The secondary anode is connected to a second amplifier and a second time to digital converter, the output of which increments a counter in the same manner as mentioned above.

It will be appreciated that the ratio of the cross-sectional area of the perforations to the total cross-sectional area of the anode can be chosen to give a particular degree of attenuation to the incoming secondary electron beam.

Thus, in use, the ion beam is directed onto the chevron pair 11,12.

This results in the generation of secondary electrons in the manner

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mentioned above. These secondary electrons emerge from the chevron pair 11,12 and are incident of the first anode 16. It is thought that by arranging for the cross-sectional area of the perforations in the first anode to be of the order of 1% of the total cross-sectional area of the anode will give the possibility for more accurate quantitative measurements over a large dynamic range, however, it is to be appreciated that the ratio of the cross-sectional area of the perforations to the total area of the anode can be of any desired magnitude in order to give appropriate attenuation characteristics.

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Therefore, if the area of the perforations represents approximately 1% of the total area of the anode, this means that 1% of the secondary electron beam which is incident on the first anode 16 will pass through that anode without being detected. This means that the intensity of any signal present at the first anode would be reduced by two orders of magnitude if measured at the second anode 18. Therefore it would be appreciated that with this arrangement, that if for example the first anode 16 can be used to detect signals of a first two orders of magnitude then the second anode, at which the signal has been reduced in intensity by a factor of 100, can be used to detect signals at a second two orders of magnitude. It will be appreciated that this allows much more accurate quantitative analysis of the incoming ion beam since signals which are above threshold will be differentiated according to their magnitude and accordingly if a signal is of such a

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magnitude as to constitute more than one ion arriving, the present arrangement will detect this and the counters will be incremented by the respective TDC's by the correct number of ions. It can clearly be seen that this will result in a significant increase in the dynamic range of the mass spectrometer.

Fig. 3 shows a variation on the embodiment of Fig. 2 in which an earthed grid 19 is positioned between the first and second anode 16 and 18. The earthed grid 19 assists in the minimisation of capacitative coupling effects between the two anodes 16 and 18.

Whilst in the embodiments of Figs. 2 and 3, attenuation of the secondary electron signal is carried out by the perforated first anode 16, attenuation can be carried out in many different ways.

Thus for example, as shown in Fig. 4, the attenuation can be carried out by wires or a grid placed in front of the first anode 16 to form the second anode 18. The cross-sectional area of the wire or grid compared to the cross-sectional area of the first plate anode is small such that a large proportion of the incident signal from the chevron pair 11,12 passes through the second anode 18 without being detected. As with the other embodiments, the attenuation can be varied by changing the cross-sectional area of the wire or grid to achieve a desired dynamic range. Furthermore, as with the other embodiments, an earthed grid 19 can be placed between the two anodes to minimise capacitative coupling of these anodes.

A further alternative is shown in Fig. 5. In this embodiment, the first anode 16, a second anode 18 and, optionally an earthed grid 19, are constructed as sandwich layers of a printed circuit board 21. The first anode 16 is formed as a perforated plate attached to a first support layer 22 which is also perforated, the perforations in the first support layer 22 being in register with the perforations in the first anode 16. Attached to the opposite side of the first support layer 22 is an earthed gird, perforations in the grid also being in register with the perforations in the first support layer 22 and the first anode 16. Attached to the opposite side of the earthed grid 19 is a second support layer 23 which carries a second anode 18 attached thereto. Fingers 24 of the second anode 18 extend through the second support layer 23 and terminate adjacent to the perforations in the earthed grid 19.

In this embodiment, the attenuation is carried out by the first anode 16 and only a proportion of the secondary electrons reach the fingers 24 of the second anode 18 through the aligned apertures. As in the previous embodiments, the earthed grid 19 minimises capacitative coupling between the two anodes.

The embodiments of Figs. 2-5 are not embodiments of mass spectrometer in accordance with the present invention.

A still further alternative is shown in Fig. 6 in which a separate attenuation element 26 of appropriate form is placed in the ion beam before the ion beam is incident on the chevron pair 11,12. The attenuation element in this embodiment, comprises a perforated plate, and is arranged

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so as to interfere only with a part of the incoming ion beam and reduces the proportion of that part of the beam which reaches the chevron pair 11,12. In this embodiment, the first anode 16 and the second anode 18 are also provided but they are provided in the same plane extending generally parallel to the longitudinal axis of the chevron pair 11,12 as spaced therefrom. Thus the attenuation element attenuates only a part of the incoming ion beam which, after passing through the chevron pair 11,12 and generating secondary electrons, is incident on the second anode 18. The unattenuated part of the incoming ion beam after passing through the chevron pair 11,12 is incident on the first anode 16. Therefore it will be appreciated that the same effect is achieved with this embodiment as is achieved in the other embodiments.

It will of course be appreciated that the overall attenuation required may also be achieved by a combination of attenuation of the incident ion beam reaching an area of the microchannel plates detector and attenuation of the secondary electron signal, for example Fig. 7.

It will further be appreciated that attenuation can be achieved by a combination of restricting the proportion of ion beam reaching a part of the chevron pair 11,12 (as in the embodiment of Fig. 6) with a restriction on the secondary electron signal emerging from the chevron pair (as in the embodiment of Fig. 4). An example of an embodiment of this type is shown in Fig. 7. In this embodiment, the incident ion beam is attenuated by a

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perforated member placed before the chevron pair 11,12. Also the secondary electron signal emerging from the chevron pair 11,12 is attenuated by placing a relatively small second anode in front of an relatively large first anode.

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It will be appreciated that it is the attenuation of the incoming ion beam or the secondary electrons ejected from the chevron pair 11,12 which allows the TDC elements to more accurately count incoming ions over a large dynamic range. The use of attenuation means that it is possible to discriminate between different magnitude above threshold signals giving rise to a more accurate quantitative analysis of the incoming ion beam and also giving rise to an extension to the dynamic range of the mass spectrometer.

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It is of course to be understood that the invention is not intended to be restricted to the details of the above embodiment which are described by way of example only.

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CLAIMS

- 1. A mass spectrometer comprising an ion source to produce ions from a substance to be detected and detector means to detect a quantity of ions incident on said detection means wherein the said detection means includes at least two detector elements, each of which elements detect at least a part of said quantity of ions from the ion source and attenuation means which acts to attenuate the quantity of ions reaching at least one said detection element, wherein at least one of said detection elements is connected to a time-to-digital converter (TDC) to allow counting of detected ions and at least one of said detection elements is connected in parallel to both a time-to-digital converter (TDC) and an analogue-to-digital converter (ADC) for ion detection.
- A mass spectrometer according to Claim 1, wherein said attenuation means also acts to attenuate secondary electrons generated by said ions incident on said detection means.
- A mass spectrometer according to Claim 1 or Claim 2, wherein each detector element comprises a separate plate anode.
- 4. A mass spectrometer according to any one of Claims 1 to 3, wherein each detector element is connected via an amplifier to a time to digital converter (TDC) to allow counting of detected ions.
- 5. A mass spectrometer according to any one of Claims 1 to 4, wherein

the detector elements are disposed one behind the other relative to the ion source.

- 6. A mass spectrometer according to any one of Claims 1 to 4, wherein the detector elements are disposed one above the other in a plane extending generally perpendicular to the direction of ion travel.
- 7. A mass spectrometer according to Claim 5, wherein an earthed grid is provided between the elements to minimise capacitative coupling between elements.
- A mass spectrometer according to any one of Claims 1 to 7, wherein the attenuation means is formed by at least one of the detector elements.
- 9. A mass spectrometer according to Claim 8, wherein the adaptation of the at least one detector comprises a plurality of perforations or other apertures in the element to allow a proportion of incident signal to pass through the element without being detected.
- 10. A mass spectrometer according to any one of claims 1 to 9, wherein said attenuation device is provided between the ion source and the detector elements which acts to reduce the number of ions reaching at least one of said elements or at least a part thereof.
- A mass spectrometer according to Claim 10, wherein the attenuation device comprises a perforated plate.
- 12. A mass spectrometer according to claim 9, wherein the cross-

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sectional area of the perforations compared to the total crosssectional area of the plate is substantially 1 to 100.

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(71) Applicant (for all designated States except US): MASS-LAB LIMITED [GB/GB]; Crewe Road, Wythenshawe, Manchester M23 9BE (GB).

(72) Inventors; and

(75) Inventors/Applicants (for US only): DAVIS, Stephen [AU/GB]; 8 Flash Lane, Bollington, Macclesfield, Cheshire SK10 5AQ (GB). MAKAROV, Alexander [RU/GB]; 80 Marlborough Avenue, Cheadle Hulme,

Cheadle, Cheshire SK8 7AR (GB). **HUGHES, Jonathan** [GB/GB]; Plum Cottage, Snelson Lane, Snelson, Macclesfield, Cheshire SK11 9BP (GB).

- (74) Agents: HILL, Richard et al.; Wilson Gunn M'Caw, 41-51 Royal Exchange, Cross Street, Manchester M2 7BD (GB).
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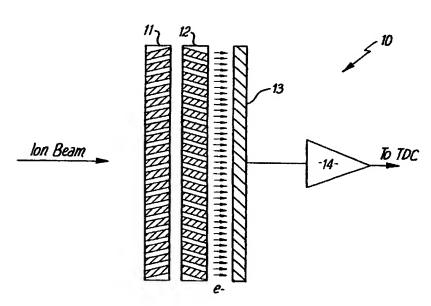
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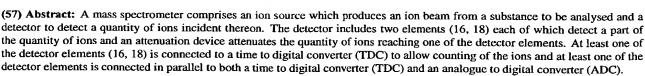
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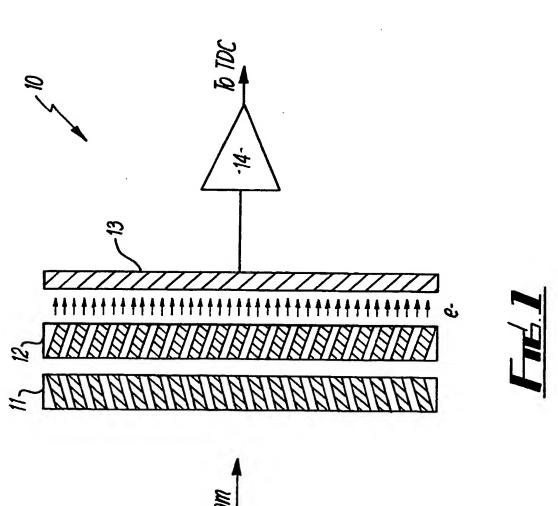




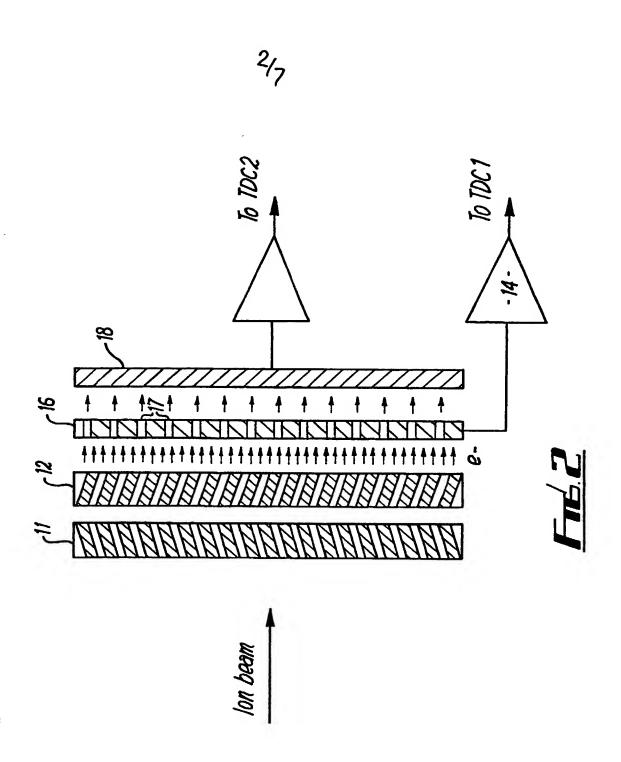




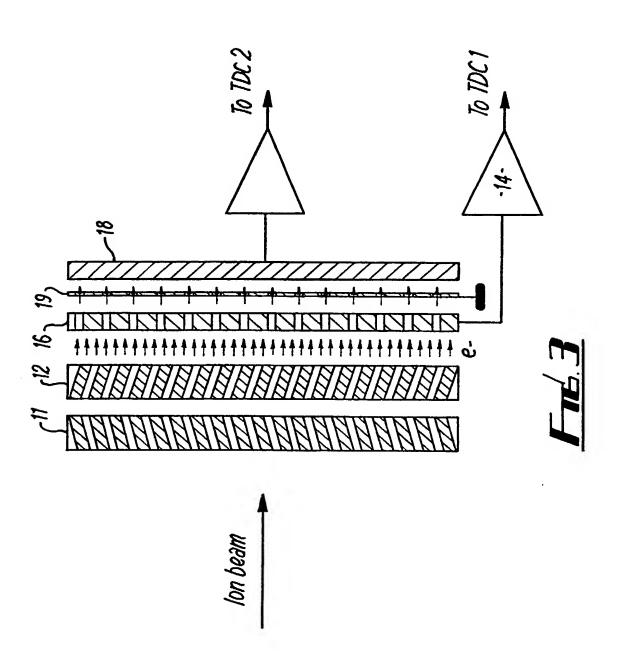
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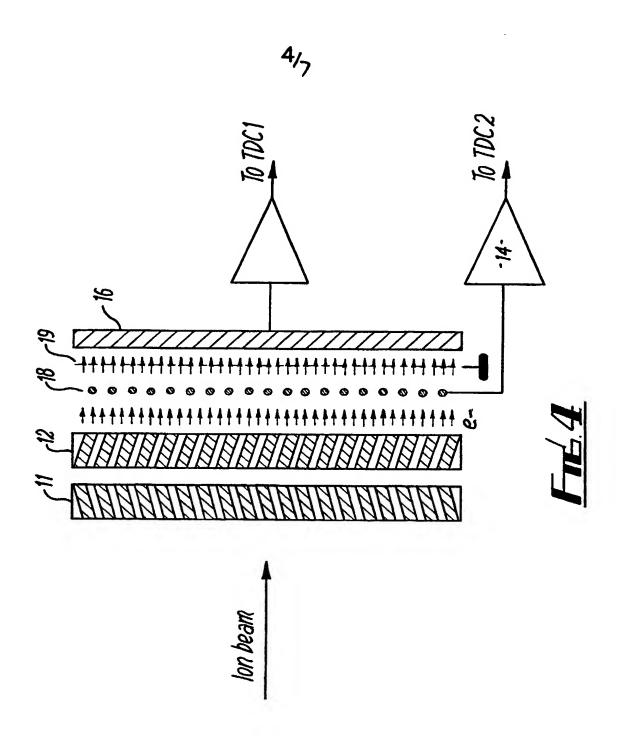
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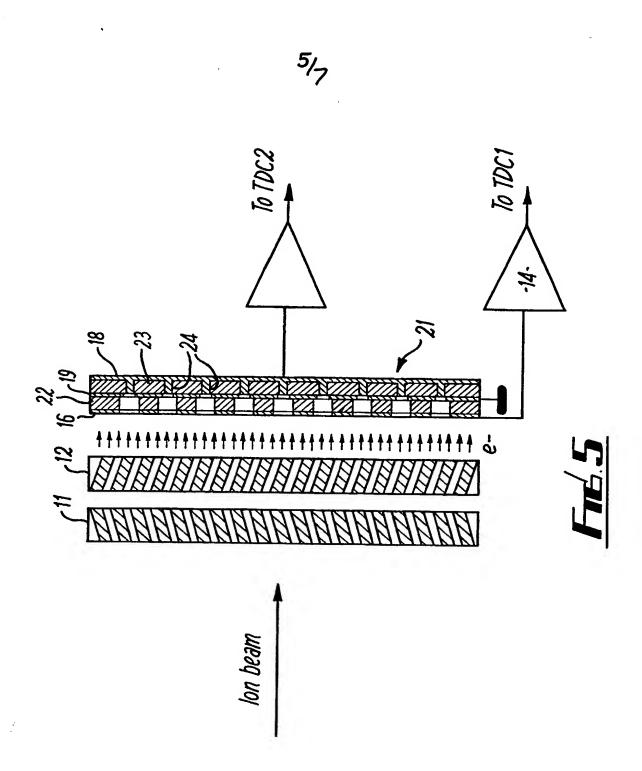


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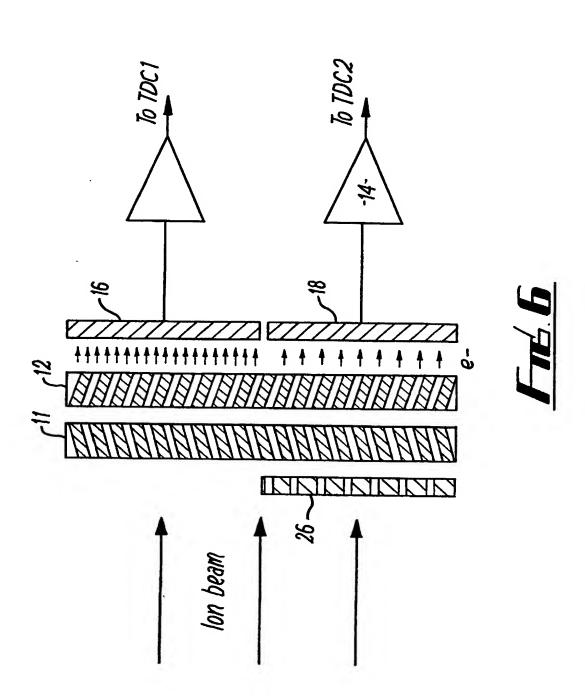


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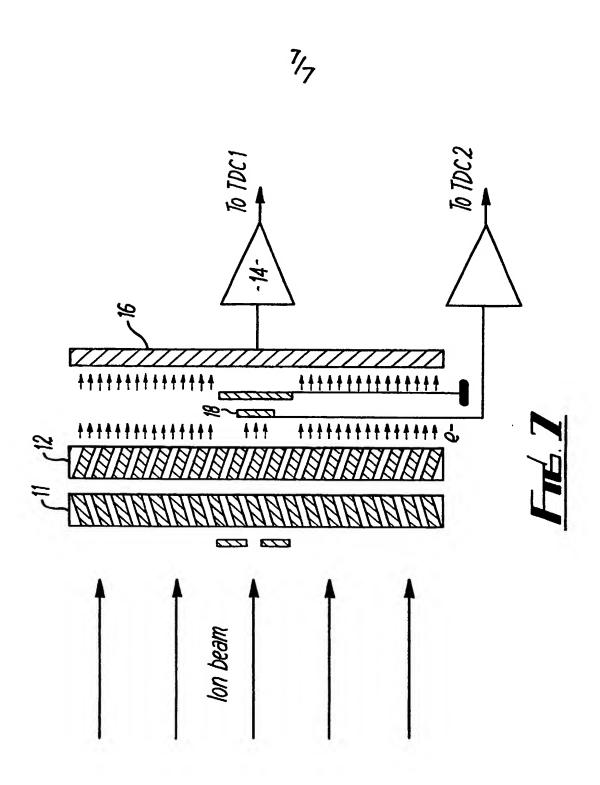




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1. 自由**报**证证



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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

POWER OF ATTORNEY FOR PATENT APPLICATION

As a representative of the Assignee, Thermo MassLab Ltd., a Limited. Company. I hereby appoint the following attorneys and/or agents to prosecute this application and transact all business in the Patent and Trademark Office connected therewith.

David L. McCombs (Reg. No. 32,271); Michael J. Balconi-Lamica (Reg. No. 34,291); Jeffrey M. Becker (Reg. No. 35,442); James R. Bell (Reg. No. 26,528); Timothy Bliss (Reg. No. 50,925); Randall C. Brown (Reg. No. 31,213); L. Howard Chen (Reg. No. 46,615); Randall E. Colson (Reg. No. 40,566); Michael A. Davis, Jr. (Reg. No. 35,488); Ruben C. DeLeon (Reg. No. 37,812); Andrew S. Ehmke (Reg. No. 50,271); Brian J. Hubbard (Reg. No. 45,873); Rita M. Irani (Reg. No. 31,028); Mark P. Kahler (Reg. No. 29,178); Warren B. Kice (Reg. No. 22,732); Christopher P. Kösh (Reg. No. 42,760); J. Andrew Lowes (Reg. No. 40,706); Todd Mattingly (Reg. No. 40,298); John Montgomery (Reg. No. 31,124); Gloria Norberg (Reg. No. 36,706); Bill R. Naifeh (Reg. No. 44,962); and David M. O'Dell (Reg. No. 42,044).



Please address all correspondence and telephone calls regarding this application to:

David L. McCombs
Attorney for Applicants
Haynes and Boone, LLP
901 Main Street, Suite 3100
Dallas, TX 75202-3789

[972] 739-8636
[972] 680-7551 - Fax

The undersigned is the representative for the Assignee of the entire right, title, and interest in the patent application identified above. A copy of the assignment or other documents in the chain of title are attached.

The undersigned (whose title is supplied below) is authorized to act on behalf of the Assignce.

	THERMO MASSLAB LTD
1/8/02	STEPHEN DAVIS
Date	Typed or printed name
	Sth. Si
	Signature
	general manager.
	Title



CUSTOMER NO. 000027683

INVENTOR'S DECLARATION FOR PATENT APPLICATION

As below named inventors, we hereby declare that:

Our residence, post office address and citizenship are as stated below next to our names;

We believe we are the original, first and sole joint inventors of the subject matter which is claimed and for which a patent is sought on the invention entitled

HIGH DYNAMIC RANGE MASS SPECTROMETER

the specific	ation of which: (check	one)					
	is attached hereto						
<u> </u>	was filed on						
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	We hereby state that we have reviewed and understand the contents of the above identified specification, ocluding the claims, as amended by any amendment referred to above.						
accordance became ava	Te acknowledge the duty to disclose information which is material to the patentability of this application in accordance with 37 CFR 1.56, including for continuation-in-part applications, material information which accorded available between the filing date of the prior application and the national or PCT international filing after the continuation-in-part application.						
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-60	FULL NAME OF INVENTOR:	Stephen DAVIS
	INVENTOR'S SIGNATURE: RESIDENCE: Macclesfield, Cheshir	0.00
	CITIZENSHIP. Australia	
	POST OFFICE ADDRESS:	8 Flash Lane, Bollington, Macclesfield, Cheshire SK10 5AQ, United Kingdom
2-50	FULL NAME OF INVENTOR:	Alexander A. MAKAROV
V	INVENTOR'S SIGNATURE:	Marayob DATED: 1/8/02 ited Kingdom GBX
	CITIZENSHIP: Russia	
	POST OFFICE ADDRESS:	80 Marlborough Avenue Cheadle Hulme, Cheadle, Cheshire SK8 7AR, United Kingdom
3-00	FULL NAME OF INVENTOR:	Jonathan HUGHES
	INVENTOR'S SIGNATURE:	DATED: 1/8/02
	RESIDENCE: Macclesfield, Cheshire	United Kingdom GBX
	CITIZENSHIP: United Kingdom	
	POST OFFICE ADDRESS:	Plum Cottage, Snelson Lane Snelson, Macclesfield, Cheshire, SK11 9BP, United Kingdom
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